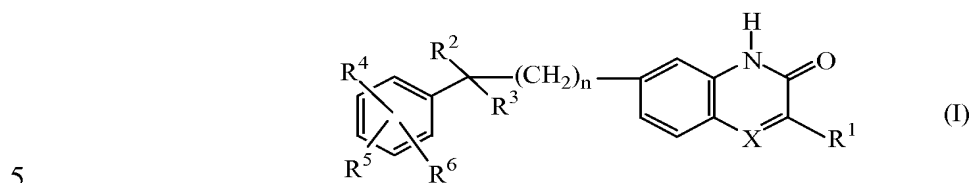


# CLAIMS

1. A compound of formula (I),



the *N*-oxide forms, the addition salts and the stereo-chemically isomeric forms thereof, wherein

10  $n$  is 0, 1 or 2;

$X$  is N or  $CR^7$ , wherein  $R^7$  is hydrogen or taken together with  $R^1$  may form a bivalent radical of formula  $-CH=CH-CH=CH-$ ;

15  $R^1$  is  $C_{1-6}$ alkyl or thienyl;

$R^2$  is hydrogen, hydroxy,  $C_{1-6}$ alkyl,  $C_{3-6}$ alkynyl or taken together with  $R^3$  may form  $=O$ ;

$R^3$  is a radical selected from

- 20
- $-(CH_2)_s- NR^8R^9$  (a-1),
  - $-O-H$  (a-2),
  - $-O-R^{10}$  (a-3),
  - $-S-R^{11}$  (a-4), or
  - $-C\equiv N$  (a-5),

25 wherein

$s$  is 0, 1, 2 or 3;

$R^8$  is  $-CHO$ ,  $C_{1-6}$ alkyl, hydroxy $C_{1-6}$ alkyl,  $C_{1-6}$ alkylcarbonyl, di( $C_{1-6}$ alkyl)amino $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy $C_{1-6}$ alkyl,  $C_{1-6}$ alkylcarbonylamino $C_{1-6}$ alkyl, piperidinyl $C_{1-6}$ alkyl, piperidinyl $C_{1-6}$ alkylaminocarbonyl,  $C_{1-6}$ alkyloxy,

30 thienyl $C_{1-6}$ alkyl, pyrrolyl $C_{1-6}$ alkyl, aryl $C_{1-6}$ alkylpiperidinyl,

arylcarbonyl $C_{1-6}$ alkyl, arylcarbonylpiperidinyl $C_{1-6}$ alkyl,

haloindozolylpiperidinyl $C_{1-6}$ alkyl, or

aryl $C_{1-6}$ alkyl( $C_{1-6}$ alkyl)amino $C_{1-6}$ alkyl;

$R^9$  is hydrogen or  $C_{1-6}$ alkyl;

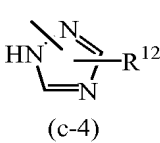
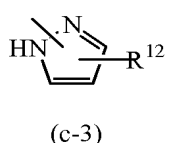
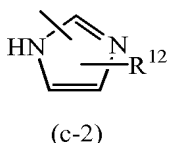
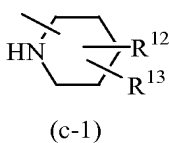
$R^{10}$  is  $C_{1-6}$ alkyl,  $C_{1-6}$ alkylcarbonyl or  $di(C_{1-6}$ alkyl)amino $C_{1-6}$ alkyl; and  
 $R^{11}$  is  $di(C_{1-6}$ alkyl)amino $C_{1-6}$ alkyl;  
or  $R^3$  is a group of formula



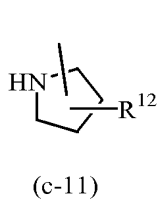
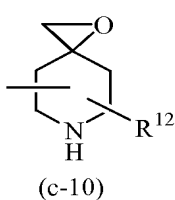
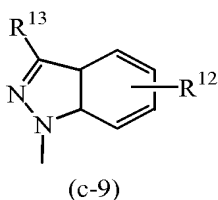
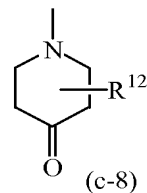
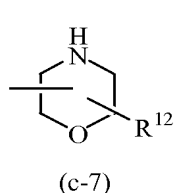
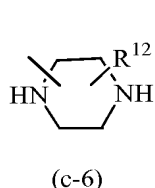
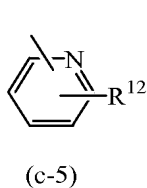
5 wherein

t is 0, 1, 2 or 3;

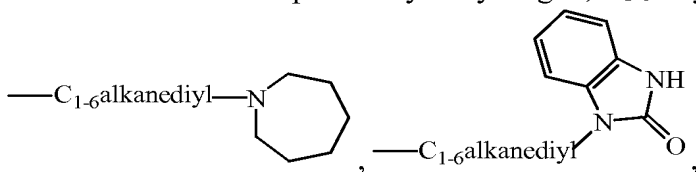
Z is a heterocyclic ring system selected from



10



15 wherein each  $R^{12}$  independently is hydrogen,  $C_{1-6}$ alkyl, aminocarbonyl, hydroxy,



$C_{1-6}$ alkyloxy $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy $C_{1-6}$ alkylamino,  $di(phenylC_{2-6}alkenyl)$ ,

piperidiny $C_{1-6}$ alkyl,  $C_{3-10}$ cycloalkyl,  $C_{3-10}$ cycloalkyl $C_{1-6}$ alkyl,

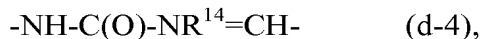
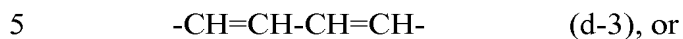
aryloxy(hydroxy) $C_{1-6}$ alkyl, haloindazolyl, aryl $C_{1-6}$ alkyl, aryl $C_{2-6}alkenyl$ , morpholino,

20  $C_{1-6}$ alkylimidazolyl, or pyridiny $C_{1-6}$ alkylamino; and

each  $R^{13}$  independently is hydrogen, piperidiny or aryl;

$R^4$ ,  $R^5$  and  $R^6$  are each independently selected from hydrogen, halo, trihalomethyl,  
trihalomethoxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy,  $di(C_{1-6}alkyl)amino$ ,  $di(C_{1-6}alkyl)aminoC_{1-6}$   
25  $alkyloxy$  or  $C_{1-6}alkyloxycarbonyl$ ; or

when R<sup>5</sup> and R<sup>6</sup> are on adjacent positions they may taken together form a bivalent radical of formula



wherein R<sup>14</sup> is C<sub>1-6</sub>alkyl;

aryl is phenyl or phenyl substituted with halo, C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkyloxy;

10

with the proviso that when

n is 0, X is N, R<sup>1</sup> is C<sub>1-6</sub>alkyl, R<sup>2</sup> is hydrogen, R<sup>3</sup> is a group of formula (b-1), t is 0, Z is the heterocyclic ring system (c-2) wherein said heterocyclic ring system Z is attached to the rest of the molecule with a nitrogen atom, and R<sup>12</sup> is hydrogen; then  
15 at least one of the substituents R<sup>4</sup>, R<sup>5</sup> or R<sup>6</sup> is other than hydrogen, halo, C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkyloxy.

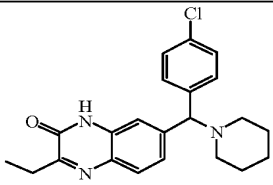
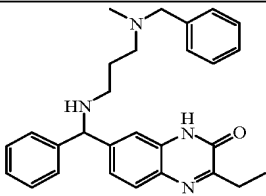
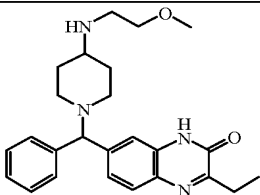
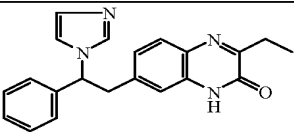
2. A compound as claimed in claim 1 wherein

n is 0 or 1; X is N or CR<sup>7</sup>, wherein R<sup>7</sup> is hydrogen; R<sup>1</sup> is C<sub>1-6</sub>alkyl; R<sup>2</sup> is hydrogen;  
20 R<sup>3</sup> is a radical selected from (a-1) or (a-2) or is group of formula (b-1); s is 0, 1 or 2;  
R<sup>8</sup> is C<sub>1-6</sub>alkyl or arylC<sub>1-6</sub>alkyl(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl; t is 0, 1 or 2; Z is a heterocyclic ring system selected from (c-1), (c-2), (c-3), (c-4), (c-5) or (c-11); each R<sup>12</sup> independently is hydrogen or C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkylamino; each R<sup>13</sup> independently is hydrogen; and R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each independently selected from  
25 hydrogen, halo or C<sub>1-6</sub>alkyl.

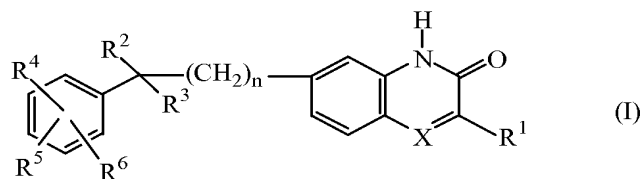
3. A compound according to claim 1 and 2 wherein

n is 0 or 1; X is N; R<sup>1</sup> is C<sub>1-6</sub>alkyl; R<sup>2</sup> is hydrogen; R<sup>3</sup> is a radical of formula (a-1) or is a group of formula (b-1); s is 0; R<sup>8</sup> is arylC<sub>1-6</sub>alkyl(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl;  
30 t is 0; Z is a heterocyclic ring system selected from (c-1) or (c-2); each R<sup>12</sup> independently is hydrogen or C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkylamino; each R<sup>13</sup> independently is hydrogen; and R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen or halo.

35 4. A compound according to claim 1, 2 and 3 selected from compound No 5, compound No 9, compound No 2 and compound No 1.

 <p>compound 5</p>	 <p>compound 9 .C<sub>2</sub>H<sub>2</sub>O<sub>4</sub> (1:2)</p>
 <p>compound 2 .C<sub>2</sub>H<sub>2</sub>O<sub>4</sub> (2:5)</p>	 <p>compound 1</p>

5. A compound as claimed in any of claims 1 to 4 for use as a medicine.
- 5 6. A pharmaceutical composition comprising pharmaceutically acceptable carriers and  
as an active ingredient a therapeutically effective amount of a compound as claimed  
in claim 1 to 4.
7. A process of preparing a pharmaceutical composition as claimed in claim 6 wherein  
10 the pharmaceutically acceptable carriers and a compound as claimed in claim 1 to 4  
are intimately mixed.
8. Use of a compound for the manufacture of a medicament for the treatment of a  
15 PARP mediated disorder, wherein said compound is a compound of formula (I)



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereo-  
chemically isomeric forms thereof, wherein

*n* is 0, 1 or 2;

X is N or CR<sup>7</sup>, wherein R<sup>7</sup> is hydrogen or taken together with R<sup>1</sup> may form a bivalent radical of formula -CH=CH-CH=CH-;

5 R<sup>1</sup> is C<sub>1-6</sub>alkyl or thienyl;

R<sup>2</sup> is hydrogen, hydroxy, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>alkynyl or taken together with R<sup>3</sup> may form =O;

R<sup>3</sup> is a radical selected from

- 10            -(CH<sub>2</sub>)<sub>s</sub>- NR<sup>8</sup>R<sup>9</sup>            (a-1),  
               -O-H                            (a-2),  
               -O-R<sup>10</sup>                        (a-3),  
               -S- R<sup>11</sup>                        (a-4), or  
               —C≡N                        (a-5),

15        wherein

s is 0, 1, 2 or 3;

R<sup>8</sup> is -CHO, C<sub>1-6</sub>alkyl, hydroxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl, di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonylaminoC<sub>1-6</sub>alkyl, piperidinylC<sub>1-6</sub>alkyl, piperidinylC<sub>1-6</sub>alkylaminocarbonyl, C<sub>1-6</sub>alkyloxy, thienylC<sub>1-6</sub>alkyl, pyrrolylC<sub>1-6</sub>alkyl, arylC<sub>1-6</sub>alkylpiperidinyl, arylcarbonylC<sub>1-6</sub>alkyl, arylcarbonylpiperidinylC<sub>1-6</sub>alkyl, haloindozolylpiperidinylC<sub>1-6</sub>alkyl, or arylC<sub>1-6</sub>alkyl(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl;

R<sup>9</sup> is hydrogen or C<sub>1-6</sub>alkyl;

25        R<sup>10</sup> is C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl or di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl; and

R<sup>11</sup> is di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl;

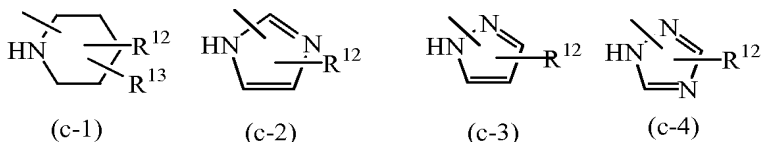
or R<sup>3</sup> is a group of formula

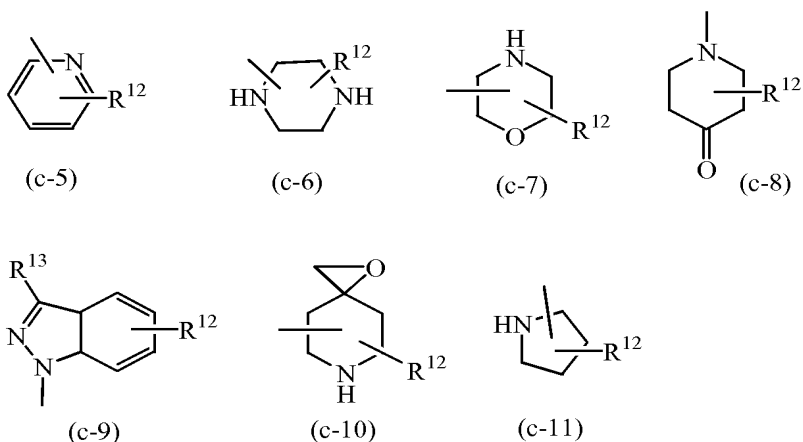


wherein

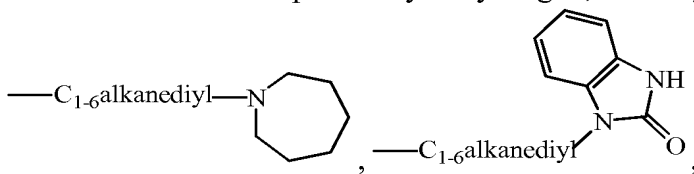
30        t is 0, 1, 2 or 3;

Z is a heterocyclic ring system selected from





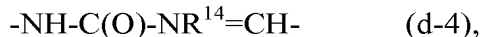
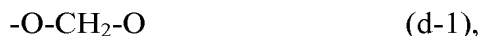
5 wherein each  $R^{12}$  independently is hydrogen,  $C_{1-6}$ alkyl, aminocarbonyl, hydroxy,



$C_{1-6}$ alkyloxy $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy $C_{1-6}$ alkylamino, di(phenyl $C_{2-6}$ alkenyl),  
 piperidinyloxy $C_{1-6}$ alkyl,  $C_{3-10}$ cycloalkyl,  $C_{3-10}$ cycloalkyl $C_{1-6}$ alkyl,  
 aryloxy(hydroxy) $C_{1-6}$ alkyl, haloindazolyl, aryl $C_{1-6}$ alkyl, aryl $C_{2-6}$ alkenyl, morpholino,  
 10  $C_{1-6}$ alkylimidazolyl, or pyridinyloxy $C_{1-6}$ alkylamino; and  
 each  $R^{13}$  independently is hydrogen, piperidinyloxy or aryl;

$R^4$ ,  $R^5$  and  $R^6$  are each independently selected from hydrogen, halo, trihalomethyl,  
 trihalomethoxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkyloxy, di( $C_{1-6}$ alkyl)amino, di( $C_{1-6}$ alkyl)amino $C_{1-6}$   
 15  $C_{1-6}$ alkyloxy or  $C_{1-6}$ alkyloxycarbonyl; or

when  $R^5$  and  $R^6$  are on adjacent positions they may taken together form a bivalent  
 radical of formula



wherein  $R^{14}$  is  $C_{1-6}$ alkyl;

aryl is phenyl or phenyl substituted with halo,  $C_{1-6}$ alkyl or  $C_{1-6}$ alkyloxy.  
 25

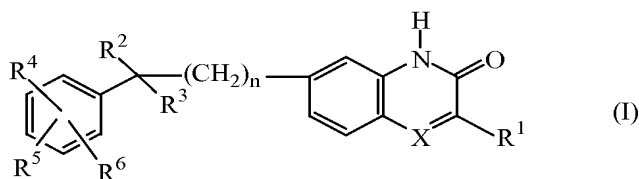
9. Use according to claim 8 of a PARP inhibitor of formula (I) for the manufacture of  
 a medicament for the treatment of a PARP-1 mediated disorder.

10. Use according to claim 8 and 9 wherein the treatment involves chemosensitization.

11. Use according to claims 8 and 9 wherein the treatment involves radiosensitization.

5

12. A combination of a compound of formula (I) with a chemotherapeutic agent



10

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

*n* is 0, 1 or 2;

15

*X* is N or CR<sup>7</sup>, wherein R<sup>7</sup> is hydrogen or taken together with R<sup>1</sup> may form a bivalent radical of formula -CH=CH-CH=CH-;

R<sup>1</sup> is C<sub>1-6</sub>alkyl or thienyl;

20

R<sup>2</sup> is hydrogen, hydroxy, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>alkynyl or taken together with R<sup>3</sup> may form =O;

R<sup>3</sup> is a radical selected from

25

-(CH<sub>2</sub>)<sub>s</sub>- NR<sup>8</sup>R<sup>9</sup> (a-1),

-O-H (a-2),

-O-R<sup>10</sup> (a-3),

-S- R<sup>11</sup> (a-4), or

—C≡N (a-5),

wherein

30

*s* is 0, 1, 2 or 3;

R<sup>8</sup>, R<sup>10</sup> and R<sup>11</sup> are each independently selected from -CHO, C<sub>1-6</sub>alkyl, hydroxyc<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarbonyl, amino, C<sub>1-6</sub>alkylamino,

di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxycarbonyl, C<sub>1-6</sub>alkylcarbonylaminoC<sub>1-6</sub>alkyl, piperidinylC<sub>1-6</sub>alkylaminocarbonyl, piperidinyl, piperidinylC<sub>1-6</sub>alkyl, piperidinylC<sub>1-6</sub>alkylaminocarbonyl, C<sub>1-6</sub>alkyloxy, thienylC<sub>1-6</sub>alkyl, pyrrolylC<sub>1-6</sub>alkyl, arylC<sub>1-6</sub>alkylpiperidinyl, arylcarbonylC<sub>1-6</sub>alkyl, arylcarbonylpiperidinylC<sub>1-6</sub>alkyl, haloindozolylpiperidinylC<sub>1-6</sub>alkyl, or arylC<sub>1-6</sub>alkyl(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyl; and R<sup>9</sup> is hydrogen or C<sub>1-6</sub>alkyl;

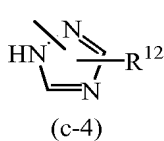
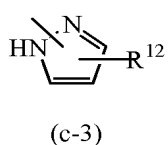
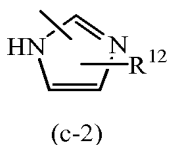
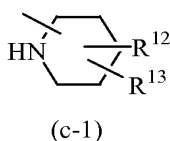
or R<sup>3</sup> is a group of formula



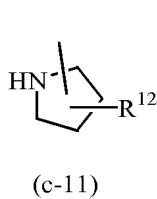
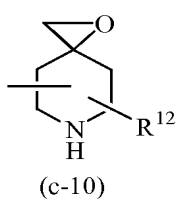
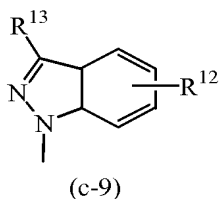
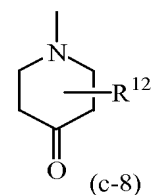
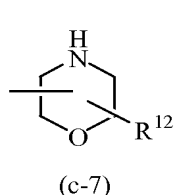
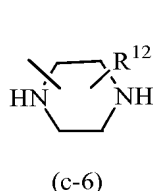
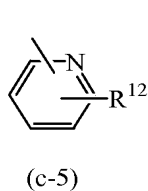
wherein

t is 0, 1, 2 or 3;

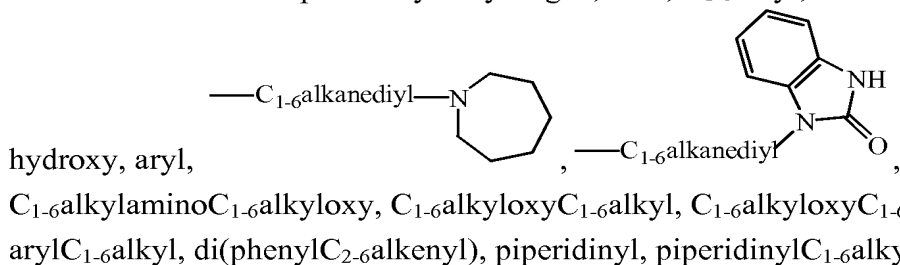
Z is a heterocyclic ring system selected from



15



20 wherein each R<sup>12</sup> independently is hydrogen, halo, C<sub>1-6</sub>alkyl, aminocarbonyl, amino,



C<sub>3-10</sub>cycloalkyl, C<sub>3-10</sub>cycloalkylC<sub>1-6</sub>alkyl, aryloxy(hydroxy)C<sub>1-6</sub>alkyl, haloindazolyl, arylC<sub>1-6</sub>alkyl, arylC<sub>2-6</sub>alkenyl, arylC<sub>1-6</sub>alkylamino, morpholino, C<sub>1-6</sub>alkylimidazolyl, or pyridinylC<sub>1-6</sub>alkylamino;

each R<sup>13</sup> independently is hydrogen, piperidinyl or aryl;

5

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen, halo, trihalomethyl, trihalomethoxy, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyloxy, amino, aminoC<sub>1-6</sub>alkyl, di(C<sub>1-6</sub>alkyl)amino, di(C<sub>1-6</sub>alkyl)aminoC<sub>1-6</sub>alkyloxy or C<sub>1-6</sub>alkyloxycarbonyl, or C<sub>1-6</sub>alkyl substituted with 1, 2 or 3 substituents independently selected from hydroxy, C<sub>1-6</sub>alkyloxy, or aminoC<sub>1-6</sub>alkyloxy; or

10

when R<sup>5</sup> and R<sup>6</sup> are on adjacent positions they may taken together form a bivalent radical of formula

-O-CH<sub>2</sub>-O (d-1),

-O-(CH<sub>2</sub>)<sub>2</sub>-O- (d-2),

15

-CH=CH-CH=CH- (d-3), or

-NH-C(O)-NR<sup>14</sup>=CH- (d-4),

wherein R<sup>14</sup> is C<sub>1-6</sub>alkyl;

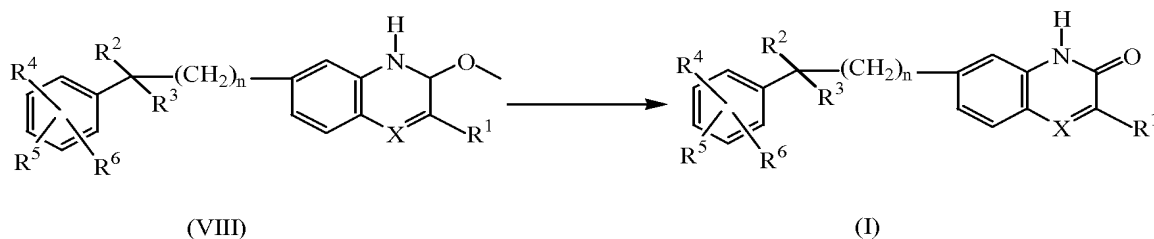
aryl is phenyl or phenyl substituted with halo, C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkyloxy.

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13. A process for preparing a compound as claimed in claim 1, characterized by

a) the hydrolysis of intermediates of formula (VIII), according to art-known methods, by submitting the intermediates of formula (VIII) to appropriate reagents, such as, tinchloride, acetic acid and hydrochloric acid, in the presence of a reaction inert solvent, e.g. tetrahydrofuran.

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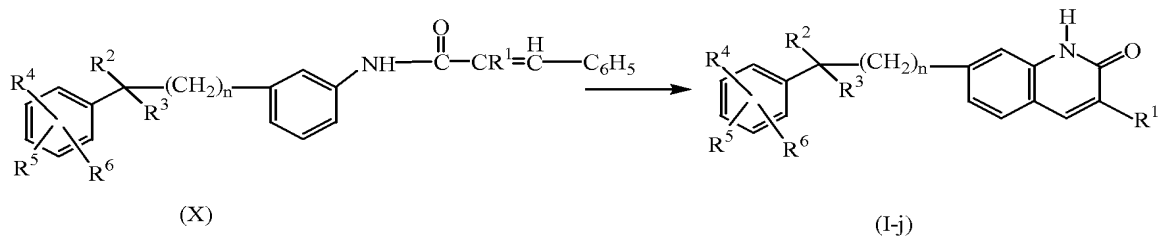


b) the cyclization of intermediates of formula (X), according to art-known cyclizing procedures into compounds of formula (I) wherein X is CH, herein referred to as compounds of formula (I-j), preferably in the presence of a suitable Lewis Acid, e.g. aluminum chloride either neat or in a suitable solvent such as, for example, an

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aromatic hydrocarbon, e.g. benzene, chlorobenzene, methylbenzene and the like;  
 halogenated hydrocarbons, e.g. trichloromethane, tetrachloromethane and the like;  
 an ether, e.g. tetrahydrofuran, 1,4-dioxane and the like or mixtures of such solvents.

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c) the condensation of an appropriate ortho-benzenediamine of formula (XI) with an  
 ester of formula (XII) wherein R<sup>h</sup> is C<sub>1-6</sub>alkyl, into compounds of formula (I),  
 10 wherein X is N, herein referred to as compounds of formula (I-i), in the presence of  
 a carboxylic acid, e.g. acetic acid and the like, a mineral acid such as, for example  
 hydrochloric acid, sulfuric acid, or a sulfonic acid such as, for example, methane-  
 sulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfonic acid and the like.

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